REMARKS

Claim Amendments

Claims 20 and 31 have been cancelled rendering the rejection under 35 USC§112, first paragraph, on page 2 of the office action moot and the new rejection under 35 USC§112, first paragraph, on page 10 of the office action moot.

Claims 15 and 16 have been amended to depend on claim 24, which defines compounds of formula I wherein B is phenyl. These amendments render moot the reasons the rejections of claim 15 and 16 under 35 U.S.C. §112, first paragraph, set forth on page 7 of the office action.

In that these amendments do not raise new issues and serve to reduce the issues on appeal, Applicants respectfully submit they are appropriate under 37 CFR §1.116.

The rejection under 35 USC §112, 1st paragraph of claims 1-13, 15-17, 20, 22, 24-31

This rejection is based on the allegation that the specification does not provide enablement for using compounds of formula I where B is naphthyl or pyridinyl. Applicants traverse this rejection and respectfully request reconsideration, particularly in view the findings of the Board of Appeals regarding a similar rejection in application no. 10/071248, now US patent no. 7528255, assigned to the same assignee as the present invention.

Claims 12, 15-17, 22, and 24-30

It is acknowledged in the office action that the specification provides enablement for using compounds of formula I where B is phenyl. Claims 12, 15-17, 22, and 24-30, define compounds and methods where B= phenyl such that the rejection of these claims should be withdrawn. Once this rejection is withdrawn, there will be no viable outstanding rejection of these claims. Therefore, Applicants respectfully submit claims 12, 15-17, 22 and 24-30 are presently allowable.

Claims 1-11 and 13

These claims are directed to compounds of formula I below and compositions thereof where B is phenyl, pyridinyl or naphthyl.

Applicants maintain no evidence has been presented to refute the teachings within the specification such that it is objectively enabling for the full scope of compounds of formula I.

The specification provides ample guidance as to how to prepare the full scope of compounds of formula I (See pages 21-29 and pages 51-127), how to prepare pharmaceutical compositions with such compounds (pages 30-40), how to administer pharmaceutical compositions with such compounds of formula I (pages 43-44) and how to test such compounds for physiological activity related to the treatment of cancers(pages 128-129).

Since the structure of the claimed ureas is clearly defined by formula I, applicants maintain one of ordinary skill in art could synthesize these ureas without undue experimentation relying only on conventional methods known in the art, such as those disclosed on page 27 of the application. The synthesis of ureas is well known such that one skilled in the art would recognize the appropriate starting materials (substituted anilines and substituted nitro-aryls) necessary to prepare the claimed compounds without any guidance from the specification. However, general preparative methods for synthesizing ureas **are** given on pages 21-26. Guidance on the selection of starting materials and reaction conditions is provided by the specific preparations of the citations provided on page 27 and further guidance is provided by the disclosure and examples that appear on pages 51-127.

Based on the disclosure within the specification and conventional methods known in the art, one of ordinary skill in the art clearly would be able to prepare the claimed compounds without undue experimentation. No evidence has been presented to the contrary.

As to using the compounds of claims 1-13, 15-17, 22, 24-30, the specification is clearly objectively enabling in disclosing that the compounds have pharmacological activity on page 1, lines 10-14; page 10, lines 3-13, pages 30-45; and are active in inhibiting raf based on the raf kinase assays disclosed on pages 127-129. It is recognized in the art that inhibition of raf kinase is correlated with the inhibition of growth of a variety of human tumor types, as discussed in citations mentioned in the specification on page 1, line 20 to page 2, line 3. Therefore, the inhibition of raf kinase correlates with the treatment of various tumors.

Examples of specific cancers (tumors) which can be treated are disclosed on pages 41-43. Dosage ranges and how to administer these compositions in the

treatment of various conditions are described on pages 43-44. The specification also provides assays for determining the activity levels of the compounds on pages 128-129. One of ordinary skill in the art by performing the same assays described in the specification or similar tests, can, by routine experimentation, determine the activity levels of each of the claimed compounds in treating the various conditions known in the art to be correlated with raf inhibition. This is absolutely routine in the field.

The distinctions in chemical properties between the phenyl rings and pyridinyl or naphthyl rings do not diminish the enabling teachings within the specification. The examiner provides no basis why one skilled in the art could not make the full scope of compounds of formula I, test the pharmacological activity (raf inhibition) of these compounds, prepare pharmaceutical compositions with these compounds, and administer these compounds.

As discussed in the previous response, ureas having naphthyl or pyridinyl groups bound directly to the urea group were known in the art and disclosed in WO 99/32436 and WO 99/32106, cited on page 27 of the specification. The synthesis methods described in these applications are similar to the syntheses disclosed in the specification and further illustrate the disclosure within the application is enabling.

Some experimentation may be required to achieve this objectives of this invention, but there is no evidence such experimentation would be undue in view of the detailed disclosure provided in the specification. Given the extent of the disclosure provided, it would at most involve routine experimentation if any at all, for one of ordinary skill in the art to make and use compounds of formula I where B is pyridinyl or naphthyl. This is clearly sufficient to satisfy the statute. See *Amgen v Hoechst Marion Roussel*, 314 F.2d 1313, 65 USPQ2d 1385 (Fed. Cir. 2003).

The examiner alleges it would require a large quantity of experimentation because these compounds would need to be synthesized and subjected to Applicant's raf biochemical assay. Given the extent of disclosure within the specification and the state of the art, these tasks would be routine.

Applicants draw attention to WO 99/32106 and WO 99/2106 to illustrate that preparing urea compounds with a pyridinyl moiety (B = pyridinyl) is possible and consistent with the teachings within the specification. Applicants agree that the examples disclosed in WO 99/32106 and WO 99/2106 are structurally distinct and provide no hint as to the activity of the compounds of formula I claimed herein.

However, the disclosures within WO 99/32106 and WO 99/2106 illustrate it would be routine to test the compounds of formula I herein for raf kinase inhibition and rebut the Examiner's assumption that the pyridinyl moiety will negatively impact raf kinase inhibition. These disclosures provide a reasonable basis to conclude that compounds where "B" is pyridinyl or naphthyl will share the same biological properties as compounds where "B" is phenyl.

Even absent the specification disclosures discussed above, the rejection of Claims 1-11 and 13 is clearly deficient in general under controlling case law. The courts have placed the burden upon the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated; see, e.g., In re Marzocchi, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971) (holding that how an enablement teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance.) The disclosure must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein. See In re Marzocchi, supra. No such evidence or reason for doubting Applicants' disclosure has been provided. Only general statements and conclusions are made regarding the guidance provided with respect to the treatment of osteoporosis and inflammation.

For the reasons stated above, Applicants maintain that they have provided more than adequate guidance to enable the claimed invention and submit all pending claims meet the requirements of 35 U.S.C. §112, first paragraph.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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